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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,711	10/22/2003	Steve J. Lackie	0654101-0018 (KinExA CIP	9771

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EXAMINER	
NGUYEN, BAO THUY L	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,711	LACKIE ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Drawings

1. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the original drawings are not legible. Some of the figures also lack units and appropriate labels. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The instant claims are drawn to an assay in which the contact time between a solid phase reactant and a sample is limited to less than about 1 second, 0.48 seconds, 0.12 seconds, and 0.06 seconds. These contact times were not disclosed in the parent applications.

3. This application repeats a substantial portion of prior Application No. 08/277,225, filed 18 July 1994, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Specification

4. The disclosure is objected to because of the following informalities: the status of the parent applications needs to be updated.

Appropriate correction is required.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

The contact times recited in Claims 1, 8 and 9 do not have support in the specification.

Claim Rejections - 35 USC § 112

5. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, part (d) the recitation of "the mixture produced in step (a) lacks antecedent support because step (a) does not recite a mixture.

The recitation of the contacting time in step (d) is confusing since it is unclear what is meant by "contacting time for a column volume of mixture". Does this mean that the time it takes for the mixture of analyte/second ligand complex to clear a column is less than about 1 second? The use of a column has not been previously defined. Furthermore, the recited contact times have not been properly explained nor recited in the specification, thus the specification does not provide antecedent support for these recited times.

Claims 8 and 9 suffers from the same problem.

Claim 5 is confusing since it is unclear how the step of mixing and combining a sample with a reagent (i.e. second ligand) influence its concentration. It would seem that the concentration of a particular reagent is dependent on how much is added.

Claim 6 is confusing because it is unclear if the recited solid phase is the same one recited in part (c) of claim 1 or if it is a different solid phase.

Claim 7 is confusing since it appears to recite that in the absence of analyte, less first ligand/second ligand complexes are formed. If the analyte and the second ligand competes for binding with the first ligand as recited in claim 1, then it would necessary follows that in the absence of analyte, more first ligand/second ligand complexes would be formed.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1 and 4-9 are rejected under 35 U.S.C. 103 as being unpatentable over Pollema et al (*Anal. Chem., 64:1356-1361, 1992*) in view of Friguet et al (*J. of Immuno. Meth., 77:305-319, 1985*) and Woods et al (U.S. Patent No. 4,469,787).

Pollema teaches a sequential immunoassay for the investigation of a short-time kinetic study of antibody binding. Pollema teaches using immunomagnetic beads as the solid phase which are coated with antibodies against the protein to be detected (page 1356, column 2). The beads are packed into a reaction coil to form an immobilized reaction surface. Next, labeled protein is aspirated into the reaction coil, and the flow is stopped for a specified contact time. This contact time can vary to cover a dynamic range from initial binding to equilibrium. The timing can be control and is about 0.1 second to investigate the kinetics of binding. Following the stopped flow, unbound portion of the sample is measured to determine the amount of unbound labeled reagent present. This yields a signal that can be related to the protein concentration. Pollema teaches the contact ranging from 5 seconds up to 2 minutes. Pollema teaches a competitive binding reaction of a serum sample by "spiking" an unlabeled antibody with a known quantity of an identical FITC-labeled antibody. First the beads are placed into the magnetic field and held; next, the spiked sample is introduced onto the beads. If the sample contains little antibody, then the spiked labeled antibody will undergo maximum binding and a small resultant signal will occur at the detector. On the other hand, if a large amount of antibody exists in the sample, than many of the active sites which would normally bind the labeled antibody will be occupied, and a large signal will be detected. This competitive assay is optimized if there is a slight excess of labeled antibodies for the sites available. Pollema also teaches that in a sandwich assay, an excess of both labeled and unlabeled antibodies are used to

drive the reaction to the maximum bound state (page 1359, column 2). Pollema teaches a variation of the competitive immunoassay in which the beads and sample were sequentially aspirated into the reaction coil and merged in the flowing stream. Following aspiration, the flow was stopped and allows the specified contact time. Measurement is taken of the unbound fraction (page 1360, column 1).

Pollema differs from the instant invention in failing to specifically teach the steps of the competitive and sandwich immunoassays, and measuring the bound label as an indication of the amount of analyte present in the sample.

Friguet, however, discloses an enzyme-linked immunosorbent assay involving mixing antigen (analyte) with an antigen-specific antibody (second ligand), contacting the resulting mixture with a solid phase coated with the antigen (first ligand), binding a detectable tag (a second antibody) to the antigen-specific antibody, and detecting the portion of the tag bound to the solid phase (bound to the first ligand/second ligand complexes on the solid phase), page 309. The method of Friguet allows detection and quantitation of solid phase bound antibody/antigen complexes and allows for indirect determination of the presence or level of analyte. Friguet teaches mixing similar concentration of analyte and antibody (page 309, lines 6-7). Friguet teaches performing the contacting step under conditions and for a time sufficiently limited that no readjustment of the liquid phase equilibrium occurs during the step of contacting the mixture with the solid phase (page 313).

And Woods teaches a method for quantitatively determining the presence of a ligand in a sample in a sandwich immunoassay (column 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method taught by Pollema to perform either a competitive or

sandwich assay as taught by Friguet because Pollema teaches that sequential injection offers several advantages for immunoassays. The highly reproducible timing obtained with sequential injection allows for accurate analysis that can extend into non-equilibrium measurements in a very short time frame not generally considered or achieved by a batch technique. Sequential injection accelerates sample handling, which in batch method is too slow thus preventing the utilization of short-time kinetics. Stop-flow techniques enhance the usefulness of immunoassay by allowing well-controlled contact times between antibody and antigen, which can range from only a fraction of a second into the traditional equilibrium time frame. The assay of Pollema can be utilized to characterize antibodies and to study kinetics of binding and quickly allow the study of the behavior of immobilized antibody. The steps involved in a sandwich and competitive assay are well known in the art as demonstrated by Friguet and Woods, and a skilled artisan can have a reasonable expectation of success using the steps taught by Friguet in the system of Pollema because Pollema teaches that the system can be used without modification to carry out a competitive assay. It is also within the skill of the ordinary artisan to modify the system of Pollema to perform a sandwich immunoassay, as taught by Woods, because such assays are well known in the art, and are suggested by Pollema as being highly sensitive.

8. Claims 2 and 3 are rejected under 35 U.S.C. 103 as being unpatentable over Pollema et al (*Anal. Chem., 64:1356-1361, 1992*) in view of Friguet et al (*J. of Immuno. Meth., 77:305-319, 1985*) and Woods et al (U.S. Patent No. 4,469,787) as applied to claims 1 and 4-9 above, and further in view of Freytag (*Clin. Chem, 30(9):1494-1498, 1984*).

See discussion of Pollema, Friguet and Woods above. These references differ from the instant invention in failing to specifically teach that the first ligand and the analyte are different.

Freytag, however, teaches an affinity column-mediated immunoassay performed under non-competitive or non-equilibrium conditions wherein an antigen different from the sample antigen, e.g. an analyte analog, is used as the solid phase bound antigen is used as a solid phase antigen in an assay (page 1496, column 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to perform the assay of Pollema as modified by Friguet and Woods using an antigen different from the sample antigen, e.g. an analyte analog, as the solid phase antigen because Friguet teaches that using analyte analogs as the immobilized antigen can yield higher assay sensitivity (page 1496, column 1).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 8:00 a.m. -3:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
9/9/04